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EXAMINER	
CROW, ROBERT THOMAS	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/693,428	ROBBINS ET AL.	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 15 June 2006 in which the Specification and claims 1, 3, 5, 9-11, 16-19, 22, and 24 were amended, claim 2 was canceled, and no claims were added. All of the amendments have been thoroughly reviewed and entered.

2. The previous rejections under 35 U.S.C. 112, second paragraph, are withdrawn in view of the amendments.

3. The previous rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103(a) not reiterated below are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are addressed following the rejections necessitated by the amendments.

4. The previous rejections under the judicially created doctrine of obviousness-type double patenting are withdrawn in view of the amendments. However, new rejections under the judicially created doctrine of obviousness-type double patenting are presented in view of the amendments and in view of Applicant's deferral of entry of a terminal disclaimer.

5. Claims 1 and 3-24 are under prosecution.

Specification

The amendment to the Specification filed 15 June 2006 is acknowledged. Receipt of the copy of the Preliminary Amendment filed 20 November 2003 is also acknowledged.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, 6, 9, 12, 14, 15, 16, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Sambrook et al (*Molecular Cloning, A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15 and pp. 7.26-7.29 (1989)) as evidenced by Utermohlen (U.S. Patent No. 5,437,976, issued 1 August 1995) and Stryer (Biochemistry, 2nd ed, W.H.Freeman and Co., New York, page 376 (1981)).

Regarding claim 1, Sambrook et al teach a method of preparing RNA substantially free of genomic DNA, comprising the following steps:

forming a lysate from a biological sample (page 7.12, step 1-page 7.14, step 11);

removing essentially all of the genomic DNA from the lysate, therein forming a sample preparation (e.g., incubating with DNAse to digest all DNA; page 7.14, steps 13-15);

forming an RNA-containing precipitate by adding an organic solvent to the sample preparation (e.g., ethanol is added to precipitate RNA; page 7.14, steps 15-18);

contacting an RNA isolation membrane column with said RNA-containing precipitate (e.g., performing oligo(dT) -cellulose type chromatography on the RNA; page 7.15, paragraph ii), wherein said column comprises a polymeric membrane (e.g., Amersham Hybond-mAP paper filters embedded with poly(U) residues [page 7.29, paragraph 2]; Utermohlen defines Hybond-mAP paper filters as comprising poly-U bound to arylamine substituted cellulose paper [column 3, lines 30-36],and Wade defines cellulose as a polymer [page 376, paragraph 5]; therefore, the Amersham Hybond-mAP paper filters are polymeric membranes) acting as a physical barrier to said RNA-containing precipitate and retaining the RNA-

containing precipitate for purification (e.g., the membrane [i.e., the Amersham Hybond-mAP paper filter] is a physical barrier[i.e., a filter] that retains RNA; page 7.29, paragraph 20; and

collecting said RNA-containing precipitate from said membrane, wherein said RNA-containing precipitate is substantially free of said genomic DNA (e.g., mRNAs are isolated; page 7.26, first paragraph).

Regarding claim 5, Sambrook et al teach the method of claim 1 wherein removing essentially all of the genomic DNA is accomplished by using a pre-filtration technique (e.g., genomic DNA is removed prior to chromatography; page 7.26, paragraph 1).

Regarding claim 6, Sambrook et al teach the method of claim 1 wherein said lysate is formed employing a lysis buffer comprising a chaotropic agent (e.g., they lysis buffer has the detergent Nonidet P-40; page 7.12, step 2).

Regarding claim 9, Sambrook et al teach the method of claim 1 wherein said biological sample is animal cells (e.g., mammalian cells; page 7.12, line 1).

Regarding claim 12, Sambrook et al teach the method of claim 1 wherein said precipitate comprises RNA essentially free of DNA (e.g., poly(A)+ RNA is selected; page 7.26, line 1).

Regarding claim 14, Sambrook et al teach the method of claim 1 wherein said organic solvent is ethanol (page 7.14, steps 13-15).

Regarding claim 15, Sambrook et al teach the method of claim 1 wherein said precipitate is washed following contact with the RNA isolation membrane column with a wash solution comprising an organic solvent (e.g., the RNA is stored in a TE buffer with ethanol prior to oligo(dT)-chromatography; page 7.14, step 18).

Regarding claim 16, Sambrook et al teach the method of claim 15 wherein said wash solution comprises ethanol (e.g., 71% final concentration of ethanol; page 7.14, step 18) and a buffering agent to maintain a pH form about 6 to about 9 (e.g., TE at pH 7.6; page 7.14, step 18).

Regarding claim 18, Sambrook et al teach the method of claim 16, wherein said wash solution comprises from about 40% to about 90% ethanol (e.g., 71% final concentration of ethanol; page 7.14, step 18) and a buffering agent to maintain a pH from about 6 to about 9 (e.g., TE at pH 7.6; page 7.14, step 18).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. Claims 1, 4-10, 12-21 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Colpan et al (U.S. Patent No. 6,383,393 B1, issued 7 May 2002) in view of Sambrook et al (*Molecular Cloning, A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15, pp. 7.26-7.29, and pp. E10-E.14 (1989)) as evidenced by Utermohlen (U.S. Patent No. 5,437,976, issued 1 August 1995) and Stryer (Biochemistry, 2nd ed, W.H.Freeman and Co., New York, page 376 (1981)).

Regarding claim 1, Colpan et al teach the method of preparing an RNA sample substantially free of genomic DNA (e.g., a method for purification and separation of nucleic acid mixtures; Abstract, lines 1-2), comprising the following steps:

forming a lysate from a biological sample (column 2, line 65);

removing essentially all genomic DNA from the lysate therein forming a sample preparation (e.g., contacting a column with said lysate [column 7, lines 30-36], RNA is separated and purified [i.e., genomic DNA is removed] by the column; column 6, lines 7-8), and forming an RNA-containing precipitate by adding an organic solvent to the sample preparation (e.g., the column is washed with a buffer containing isopropanol [Example 1, column 8, lines 4-10] wherein the nucleic acids are precipitated on the surface of the glass fibers [column 2, lines 12-17] and collecting the effluent from said column, wherein said effluent is substantially free of said genomic DNA [i.e., RNA is purified]; column 6, lines 4-8).

While Colpan et al also teach use of the nucleic acid subsequent reactions (column 4, lines 15-21), Colpan et al are silent with respect to an RNA isolation membrane column.

However, Sambrook et al teach a method of purifying RNA (e.g., poly(A)+ RNA; page 7.26, line 1) using RNA free of genomic DNA (page 7.12-page 7.15), wherein total cytoplasmic RNA is precipitated after removal of genomic DNA to form an RNA-containing precipitate (e.g., gDNA is removed prior to chromatography [page 7.26, paragraph 1] and ethanol is added to precipitate RNA; page 7.14, steps 15-18) with the added benefit that precipitation is a rapid and quantitative method for concentrating nucleic acids (page E10, first paragraph).

Sambrook et al also teach contacting an RNA isolation membrane column with said RNA-containing precipitate (e.g., performing oligo(dT) -cellulose type chromatography on the RNA; page 7.15, paragraph ii), wherein said column comprises a polymeric membrane (e.g., Amersham Hybond-mAP paper filters embedded with poly(U) residues [page 7.29, paragraph 2]; Utermohlen defines Hybond-mAP paper filters as comprising poly-U bound to arylamine substituted cellulose paper [column 3, lines

30-36],and Wade defines cellulose as a polymer [page 376, paragraph 5]; therefore, the Amersham Hybond-mAP paper filters are polymeric membranes) acting as a physical barrier to said RNA-containing precipitate and retaining the RNA-containing precipitate for purification (e.g., the membrane [i.e., the Amersham Hybond-mAP paper filter] is a physical barrier[i.e., a filter] that retains RNA; page 7.29, paragraph 20; and

collecting said RNA-containing precipitate from said membrane, wherein said RNA-containing precipitate is substantially free of said genomic DNA (e.g., mRNAs are isolated; page 7.26, first paragraph) with the added benefit that the RNA isolation column allows for the essential step of preparing mRNA for use in construction of cDNA libraries (page 7.26, first paragraph).

It would therefore have been obvious to modify the method of preparing an RNA sample as taught by Colpan et al with the precipitation and purification steps as taught by Sambrook et al as evidenced by Utermohlen and Stryer with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in rapid and quantitative concentration of the nucleic acid and would also have fulfilled the essential step of preparing mRNA for use in construction of cDNA libraries as explicitly taught by Sambrook et al (page E10, first paragraph and page 7.26, first paragraph).

Regarding claim 4, the method of claim 1 is discussed above. Colpan et al also teach fiber material having a particle retention ranging from about 0.1 microns to about 10 microns (e.g., the glass has a pore size of 1 micron; column 6, lines 60-67).

Regarding claim 5, the method of claim 1 is discussed above. Colpan et al also teach removing essentially all of the gDNA using a prefiltration technique (e.g., RNA is separated and purified by the column; column 6, lines 7-8).

Regarding claim 6, the method of claim 1 is discussed above. Colpan et al also teach chaotropic reagent in the preparation of the lysate (column 3, lines 1-8).

Regarding claim 7, the method of claim 6 is discussed above. Colpan et al also teach the chaotropic reagent guanidine hydrochloride (column 7, lines 60-67).

Regarding claim 8, the method of claim 7 is discussed above. Colpan et al also teach concentrations of chaotropic reagents ranging from about 0.5 M to about 5.0 M (Example 1, column 7, lines 64-66).

Regarding claim 9, the method of claim 1 is discussed above. Colpan et al also teach said biological sample are cells (column 5, lines 64-67).

Regarding claim 10, the method of claim 9 is discussed above. Colpan et al also teach said cells are blood (column 5, lines 64-67).

Regarding claim 12, the method of claim 9 is discussed above. Colpan et al also teach RNA essentially free of DNA (e.g., RNA is separated and purified by the column; column 6, lines 7-8).

Regarding claim 13, the method of claim 1 is discussed above. Colpan et al also teach lysis buffers comprising beta-mercaptoethanol (column 11, lines 62-67).

Regarding claim 14, the method of claim 1 is discussed above. Colpan et al also teach the organic solvent is isopropanol (e.g., the column is washed with a buffer containing isopropanol; Example 1, column 8, lines 4-10)

Regarding claim 15, the method of claim 1 is discussed above. Colpan et al also teach washing the precipitate with a wash solution comprising an organic solvent (e.g., the nucleic acids precipitated on the column [column 2, lines 12-17] are washed with 80%ethanol/water; column 8, lines 10-15).

Regarding claim 16, the method of claim 15 is discussed above. Colpan et al also teach washing the precipitate with wash solutions comprising ethanol and a buffering agent to maintain a pH from about 6 to about 9 (e.g., the nucleic acids precipitated on the column [column 2, lines 12-17] are washed with TrisHCl [pH 7.5] and 30-80% ethanol; column 9, lines 33-38).

Regarding claim 17, the method of claim 16 is discussed above. Colpan et al also teach wash solutions comprising from about 0.2 to about 2M guanidine, from about 5 to about 25% ethanol, and a buffering agent to maintain a pH from about 6 to about 9 (e.g., Example 7, column 9, lines 10-33).

Regarding claim 18, the method of claim 16 is discussed above. Colpan et al also teach wash solutions comprising about 40 to about 90% ethanol and a buffering agent to maintain a pH from about 6 to about 9 (e.g., TrisHCl (pH 7.5) and 30-80% ethanol; column 9, lines 33-38).

Regarding claim 19, Colpan et al teach the method of preparing a sample substantially free of genomic DNA (e.g., a method for purification and separation of nucleic acid mixtures; Abstract, lines 1-2), comprising the following steps:

forming a lysate from a biological sample (column 2, line 65);

contacting a pre-filtration column with said lysate (column 7, lines 30-36), wherein said pre-filtration column comprises a fiber material, wherein said fiber material has at least one layer of glass (column 7, lines 30-36), and whereby essentially all genomic DNA in said lysate is removed to produce a filtrate (e.g., RNA is separated and purified [i.e., genomic DNA is removed] by the column; column 6, lines 7-8); and forming an RNA-containing precipitate by adding an organic solvent to the said filtrate (e.g., the column is washed with a buffer containing isopropanol [Example 1, column 8, lines 4-10] wherein the nucleic acids are precipitated on the surface of the glass fibers [column 2, lines 12-17] and collecting the effluent from said column, wherein said effluent is substantially free of said genomic DNA [i.e., RNA is purified]; column 6, lines 4-8)).

While Colpan et al teach the use of a column to purify RNA (column 6, lines 10-12), Colpan et al are silent with respect to an RNA-isolation membrane column.

However, Sambrook et al teach a method of purifying RNA (e.g., poly(A)+ RNA; page 7.26, line 1) using RNA free of genomic DNA (page 7.12-page 7.15), wherein total cytoplasmic RNA is precipitated after removal of genomic DNA (e.g., gDNA is removed by precipitation [page 7.15, paragraph ii] prior to

chromatography; page 7.26, paragraph 1) with the added benefit that precipitation is a rapid and quantitative method for concentrating nucleic acids (page E10, first paragraph).

Sambrook et al also teach contacting an RNA isolation membrane column with said RNA-containing precipitate (e.g., performing oligo(dT) -cellulose type chromatography on the RNA; page 7.15, paragraph ii), wherein said column comprises a polymeric RNA isolation membrane (e.g., Amersham Hybond-mAP paper filters embedded with poly(U) residues [page 7.29, paragraph 2]; Utermohlen defines Hybond-mAP paper filters as comprising poly-U bound to arylamine substituted cellulose paper [column 3, lines 30-36],and Wade defines cellulose as a polymer [page 376, paragraph 5]; therefore, the Amersham Hybond-mAP paper filters are polymeric membranes) acting as a physical barrier to said RNA-containing precipitate and retaining the RNA-containing precipitate for purification (e.g., the membrane [i.e., the Amersham Hybond-mAP paper filter] is a physical barrier[i.e., a filter] that retains RNA; page 7.29, paragraph 20; and

collecting said RNA-containing precipitate from said membrane, wherein said RNA-containing precipitate is substantially free of said genomic DNA (e.g., mRNAs are isolated; page 7.26, first paragraph) with the added benefit that the RNA isolation column allows for the essential step of preparing mRNA for use in construction of cDNA libraries (page 7.26, first paragraph).

It would therefore have been obvious to modify the method of preparing an RNA sample as taught by Colpan et al with the precipitation and purification steps as taught by Sambrook et al as evidenced by Utermohlen and Stryer with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in rapid and quantitative concentration of the nucleic acid and would also have fulfilled the essential step of preparing mRNA for use in construction of cDNA libraries as explicitly taught by Sambrook et al (page E10, first paragraph and page 7.26, first paragraph).

Regarding claim 20, the method of claim 19 is discussed above. Colpan et al also teach fiber material having a particle retention ranging from about 0.1 microns to about 10 microns (e.g., the glass has a pore size of 1 micron; column 6, lines 60-67).

Regarding claim 21, the method of claim 19 is discussed above. Colpan et al also teach fiber material having a thickness ranging from about 50 microns to about 2000 microns (column 6, lines 60-67).

Regarding claim 23, the method of claim 19 is discussed above. While Sambrook et al teach membranes in RNA isolation columns (e.g., paper filters embedded with poly(U) residues; page 7.29, paragraph 2), Sambrook et al do not teach the particle retention of said membranes. However, column membranes with particle retention ranging from about 0.1 to about 10 microns were well known in the art at the time the invention was claimed, as evidenced by the teaching of Colpan et al, wherein column membranes with particle retention in the micron range (e.g., membranes having pore sizes of about 5 microns; column 6, lines 44-51) are disclosed as having the added advantage of allowing lysate components to pass through without obstruction (column 6, lines 44-47).

3. Claims 19, 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Colpan et al (U.S. Patent No. 6,383,393 B1, issued 7 May 2002) and Sambrook et al (*Molecular Cloning, A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15, pp. 7.26-7.29, and pp. E10-E.14 (1989)) as evidenced by Utermohlen (U.S. Patent No. 5,437,976, issued 1 August 1995), Stryer (Biochemistry, 2nd ed, W.H.Freeman and Co., New York, page 376 (1981)), and the Aldrich Catalog (Aldrich Chemical Company, Milwaukee, WI, page T281 (1998/1999)).

Regarding claim 22, Colpan et al teach the method of claim 19 of preparing a sample substantially free of genomic DNA (e.g., a method for purification and separation of nucleic acid mixtures; Abstract, lines 1-2), comprising the following steps:

forming a lysate from a biological sample (column 2, line 65);

contacting a pre-filtration column with said lysate (column 7, lines 30-36), wherein said pre-filtration column comprises a fiber material, wherein said fiber material has at least one layer of glass (column 7, lines 30-36), and whereby essentially all genomic DNA in said lysate is removed to produce a filtrate (e.g., RNA is separated and purified [i.e., genomic DNA is removed] by the column; column 6, lines 7-8); and forming an RNA-containing precipitate by adding an organic solvent to the said filtrate (e.g., the column is washed with a buffer containing isopropanol [Example 1, column 8, lines 4-10] wherein the nucleic acids are precipitated on the surface of the glass fibers [column 2, lines 12-17] and collecting the effluent from said column, wherein said effluent is substantially free of said genomic DNA [i.e., RNA is purified]; column 6, lines 4-8)).

While Colpan et al teach the use of a column to purify RNA (column 6, lines 10-12), Colpan et al are silent with respect to an RNA isolation membrane column.

However, Sambrook et al teach a method of purifying RNA (e.g., poly(A)+ RNA; page 7.26, line 1) using RNA free of genomic DNA (page 7.12-page 7.15), wherein total cytoplasmic RNA is precipitated after removal of genomic DNA (e.g., gDNA is removed by precipitation [page 7.15, paragraph ii] prior to chromatography; page 7.26, paragraph 1) with the added benefit that precipitation is a rapid and quantitative method for concentrating nucleic acids (page E10, first paragraph).

Sambrook et al also teach contacting an RNA isolation membrane column with said RNA-containing precipitate (e.g., performing oligo(dT) -cellulose type chromatography on the RNA; page 7.15, paragraph ii), wherein said column comprises a polymeric RNA isolation membrane (e.g., Amersham Hybond-mAP paper filters embedded with poly(U) residues [page 7.29, paragraph 2]; Utermohlen defines Hybond-mAP paper filters as comprising poly-U bound to arylamine substituted cellulose paper [column 3, lines 30-36],and Wade defines cellulose as a polymer [page 376, paragraph 5]; therefore, the Amersham Hybond-mAP paper filters are polymeric membranes) acting as a physical barrier to said RNA-containing precipitate and retaining the RNA-containing precipitate for purification (e.g., the

membrane [i.e., the Amersham Hybond-mAP paper filter] is a physical barrier[i.e., a filter] that retains RNA; page 7.29, paragraph 20; and

collecting said RNA-containing precipitate from said membrane, wherein said RNA-containing precipitate is substantially free of said genomic DNA (e.g., mRNAs are isolated; page 7.26, first paragraph) with the added benefit that the RNA isolation column allows for the essential step of preparing mRNA for use in construction of cDNA libraries (page 7.26, first paragraph).

It would therefore have been obvious to modify the method of preparing an RNA sample as taught by Colpan et al with the precipitation and purification steps as taught by Sambrook et al as evidenced by Utermohlen and Stryer with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in rapid and quantitative concentration of the nucleic acid and would also have fulfilled the essential step of preparing mRNA for use in construction of cDNA libraries as explicitly taught by Sambrook et al (page E10, first paragraph and page 7.26, first paragraph).

Colpan et al also teach the glass fiber material of claim 21, wherein the glass fiber material has a thickness ranging from about 50 microns to about 2000 microns (column 6, lines 60-67). Neither Colpan et al nor Sambrook et al teach the specific weights of the fiber material.

Aldrich teaches glass fibers in 2 in diameter bundles that are 22 feet long, weighing 454 g (page T281, column 2, paragraph 1). A filter layer having a 2 in (5.08 cm) diameter has an area of 0.00203 m^2; therefore, a filter layer having a 2 in diameter and a length (i.e., the thickness of the layer in a column) of 0.25 in has a specific weight of 212 g/m^2, thereby meeting the limitation of the claim. Further, it is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not posses characteristic relied on" (205 USPQ 594, second column, first full paragraph). In the instant case,

Applicant must provide proof that the specific weight ranging from about 75 g/m^2 to about 300 g/m^2 as claimed represents a new and non-obvious property beyond what is commonly known in the art.

4. Claims 1, 3, 19, and 24 rejected under 35 U.S.C. 103(a) as being unpatentable over Colpan et al (U.S. Patent No. 6,383,393 B1, issued 7 May 2002) and Sambrook et al (*Molecular Cloning, A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15, pp. 7.26-7.29, and pp. E10-E.14 (1989)) in view of Utermohlen (U.S. Patent No. 5,437,976, issued 1 August 1995) and as evidenced by Utermohlen (U.S. Patent No. 5,437,976, issued 1 August 1995) and Stryer (Biochemistry, 2nd ed, W.H.Freeman and Co., New York, page 376 (1981)).

Regarding claim 3, Colpan et al teach the method of claim 1 of preparing an RNA sample substantially free of genomic DNA (e.g., a method for purification and separation of nucleic acid mixtures; Abstract, lines 1-2), comprising the following steps:

forming a lysate from a biological sample (column 2, line 65);

removing essentially all genomic DNA from the lysate therein forming a sample preparation (e.g., contacting a column with said lysate [column 7, lines 30-36], RNA is separated and purified [i.e., genomic DNA is removed] by the column; column 6, lines 7-8), and forming an RNA-containing precipitate by adding an organic solvent to the sample preparation (e.g., the column is washed with a buffer containing isopropanol [Example 1, column 8, lines 4-10] wherein the nucleic acids are precipitated on the surface of the glass fibers [column 2, lines 12-17] and collecting the effluent from said column, wherein said effluent is substantially free of said genomic DNA [i.e., RNA is purified]; column 6, lines 4-8).

While Colpan et al also teach use of the nucleic acid subsequent reactions (column 4, lines 15-21), Colpan et al are silent with respect to an RNA-isolation membrane column.

However, Sambrook et al teach a method of purifying RNA (e.g., poly(A)+ RNA; page 7.26, line 1) using RNA free of genomic DNA (page 7.12-page 7.15), wherein total cytoplasmic RNA is precipitated

after removal of genomic DNA to form an RNA-containing precipitate (e.g., gDNA is removed prior to chromatography [page 7.26, paragraph 1] and ethanol is added to precipitate RNA; page 7.14, steps 15-18) with the added benefit that precipitation is a rapid and quantitative method for concentrating nucleic acids (page E10, first paragraph).

Sambrook et al also teach contacting an RNA isolation membrane column with said RNA-containing precipitate (e.g., performing oligo(dT) -cellulose type chromatography on the RNA; page 7.15, paragraph ii), wherein said column comprises a polymeric membrane (e.g., Amersham Hybond-mAP paper filters embedded with poly(U) residues [page 7.29, paragraph 2]; Utermohlen defines Hybond-mAP paper filters as comprising poly-U bound to arylamine substituted cellulose paper [column 3, lines 30-36],and Wade defines cellulose as a polymer [page 376, paragraph 5]; therefore, the Amersham Hybond-mAP paper filters are polymeric membranes) acting as a physical barrier to said RNA-containing precipitate and retaining the RNA-containing precipitate for purification (e.g., the membrane [i.e., the Amersham Hybond-mAP paper filter] is a physical barrier[i.e., a filter] that retains RNA; page 7.29, paragraph 20; and

collecting said RNA-containing precipitate from said membrane, wherein said RNA-containing precipitate is substantially free of said genomic DNA (e.g., mRNAs are isolated; page 7.26, first paragraph) with the added benefit that the RNA isolation column allows for the essential step of preparing mRNA for use in construction of cDNA libraries (page 7.26, first paragraph).

It would therefore have been obvious to modify the method of preparing an RNA sample as taught by Colpan et al with the precipitation and purification steps as taught by Sambrook et al as evidenced by Utermohlen and Stryer with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in rapid and quantitative concentration of the nucleic acid and would also have fulfilled the essential step of preparing mRNA for use in construction of cDNA libraries as explicitly taught by Sambrook et al (page E10, first paragraph and page 7.26, first paragraph).

Colpan et al and Sambrook et al are silent with respect to nylon membranes.

However, Utermohlen et al teach mRNA affinity chromatography (Abstract, lines 3-5) using woven nylon matrices attached to poly(dT) (column 5, lines 52-59) having the added advantage of use as a priming matrix for cDNA synthesis (column 4, lines 8-11).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the RNA purification method as taught by Colpan et al and Sambrook et al as evidenced by Utermohlen and Stryer with the nylon matrices as taught by Utermohlen with a reasonable expectation of success. The ordinary artisan would have made such a modification because the modification would have resulted in additional use of the matrices as a priming matrix for cDNA synthesis as explicitly taught by Utermohlen (column 4, lines 8-11).

Regarding claim 24, Colpan et al teach the method of claim 19 of preparing a sample substantially free of genomic DNA (e.g., a method for purification and separation of nucleic acid mixtures; Abstract, lines 1-2), comprising the following steps:

forming a lysate from a biological sample (column 2, line 65);

contacting a pre-filtration column with said lysate (column 7, lines 30-36), wherein said pre-filtration column comprises a fiber material, wherein said fiber material has at least one layer of glass (column 7, lines 30-36), and whereby essentially all genomic DNA in said lysate is removed to produce a filtrate (e.g., RNA is separated and purified [i.e., genomic DNA is removed] by the column; column 6, lines 7-8); and forming an RNA-containing precipitate by adding an organic solvent to the said filtrate (e.g., the column is washed with a buffer containing isopropanol [Example 1, column 8, lines 4-10] wherein the nucleic acids are precipitated on the surface of the glass fibers [column 2, lines 12-17] and collecting the effluent from said column, wherein said effluent is substantially free of said genomic DNA [i.e., RNA is purified]; column 6, lines 4-8)).

While Colpan et al teach the use of a column to purify RNA (column 6, lines 10-12), Colpan et al are silent with respect to an RNA-isolation membrane column.

However, Sambrook et al teach a method of purifying RNA (e.g., poly(A)+ RNA; page 7.26, line 1) using RNA free of genomic DNA (page 7.12-page 7.15), wherein total cytoplasmic RNA is precipitated after removal of genomic DNA (e.g., gDNA is removed by precipitation [page 7.15, paragraph ii] prior to chromatography; page 7.26, paragraph 1) with the added benefit that precipitation is a rapid and quantitative method for concentrating nucleic acids (page E10, first paragraph).

Sambrook et al also teach contacting an RNA isolation membrane column with said RNA-containing precipitate (e.g., performing oligo(dT) -cellulose type chromatography on the RNA; page 7.15, paragraph ii), wherein said column comprises a polymeric RNA isolation membrane (e.g., Amersham Hybond-mAP paper filters embedded with poly(U) residues [page 7.29, paragraph 2]; Utermohlen defines Hybond-mAP paper filters as comprising poly-U bound to arylamine substituted cellulose paper [column 3, lines 30-36],and Wade defines cellulose as a polymer [page 376, paragraph 5]; therefore, the Amersham Hybond-mAP paper filters are polymeric membranes) acting as a physical barrier to said RNA-containing precipitate and retaining the RNA-containing precipitate for purification (e.g., the membrane [i.e., the Amersham Hybond-mAP paper filter] is a physical barrier[i.e., a filter] that retains RNA; page 7.29, paragraph 20; and

collecting said RNA-containing precipitate from said membrane, wherein said RNA-containing precipitate is substantially free of said genomic DNA (e.g., mRNAs are isolated; page 7.26, first paragraph) with the added benefit that the RNA isolation column allows for the essential step of preparing mRNA for use in construction of cDNA libraries (page 7.26, first paragraph).

It would therefore have been obvious to modify the method of preparing an RNA sample as taught by Colpan et al with the precipitation and purification steps as taught by Sambrook et al as evidenced by Utermohlen and Stryer with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in rapid and quantitative concentration of the nucleic acid and would also have fulfilled the essential step

of preparing mRNA for use in construction of cDNA libraries as explicitly taught by Sambrook et al (page E10, first paragraph and page 7.26, first paragraph).

Colpan et al and Sambrook et al are silent with respect to nylon membranes.

However, Utermohlen et al teach mRNA affinity chromatography (Abstract, lines 3-5) using woven nylon matrices attached to poly(dT) (column 5, lines 52-59) having the added advantage of use as a priming matrix for cDNA synthesis (column 4, lines 8-11).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the RNA purification method as taught by Colpan et al and Sambrook et al as evidenced by Utermohlen and Stryer with the nylon matrices as taught by Utermohlen with a reasonable expectation of success. The ordinary artisan would have made such a modification because the modification would have resulted in additional use of the matrices as a priming matrix for cDNA synthesis as explicitly taught by Utermohlen (column 4, lines 8-11).

5. Claims 1 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Colpan et al (U.S. Patent No. 6,383,393 B1, issued 7 May 2002) Sambrook et al (*Molecular Cloning, A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15, pp. 7.26-7.29, and pp. E10-E.14 (1989))in view of Crossway et al (U.S. Patent No. 4,996,144, issued 26 February, 1991) and as evidenced by Utermohlen (U.S. Patent No. 5,437,976, issued 1 August 1995) and Stryer (Biochemistry, 2nd ed, W.H.Freeman and Co., New York, page 376 (1981)).

Regarding claim 11, Colpan et al teach the method of claim 1 of preparing an RNA sample substantially free of genomic DNA (e.g., a method for purification and separation of nucleic acid mixtures; Abstract, lines 1-2), comprising the following steps:

forming a lysate from a biological sample (column 2, line 65);

removing essentially all genomic DNA from the lysate therein forming a sample preparation (e.g., contacting a column with said lysate [column 7, lines 30-36], RNA is separated and purified [i.e.,

genomic DNA is removed] by the column; column 6, lines 7-8), and forming an RNA-containing precipitate by adding an organic solvent to the sample preparation (e.g., the column is washed with a buffer containing isopropanol [Example 1, column 8, lines 4-10] wherein the nucleic acids are precipitated on the surface of the glass fibers [column 2, lines 12-17] and collecting the effluent from said column, wherein said effluent is substantially free of said genomic DNA [i.e., RNA is purified]; column 6, lines 4-8).

While Colpan et al also teach use of the nucleic acid subsequent reactions (column 4, lines 15-21), Colpan et al are silent with respect to an RNA isolation membrane column.

However, Sambrook et al teach a method of purifying RNA (e.g., poly(A)+ RNA; page 7.26, line 1) using RNA free of genomic DNA (page 7.12-page 7.15), wherein total cytoplasmic RNA is precipitated after removal of genomic DNA to form an RNA-containing precipitate (e.g., gDNA is removed prior to chromatography [page 7.26, paragraph 1] and ethanol is added to precipitate RNA; page 7.14, steps 15-18) with the added benefit that precipitation is a rapid and quantitative method for concentrating nucleic acids (page E10, first paragraph).

Sambrook et al also teach contacting an RNA isolation membrane column with said RNA-containing precipitate (e.g., performing oligo(dT) -cellulose type chromatography on the RNA; page 7.15, paragraph ii), wherein said column comprises a polymeric membrane (e.g., Amersham Hybond-mAP paper filters embedded with poly(U) residues [page 7.29, paragraph 2]; Utermohlen defines Hybond-mAP paper filters as comprising poly-U bound to arylamine substituted cellulose paper [column 3, lines 30-36],and Wade defines cellulose as a polymer [page 376, paragraph 5]; therefore, the Amersham Hybond-mAP paper filters are polymeric membranes) acting as a physical barrier to said RNA-containing precipitate and retaining the RNA-containing precipitate for purification (e.g., the membrane [i.e., the Amersham Hybond-mAP paper filter] is a physical barrier[i.e., a filter] that retains RNA; page 7.29, paragraph 20; and

collecting said RNA-containing precipitate from said membrane, wherein said RNA-containing precipitate is substantially free of said genomic DNA (e.g., mRNAs are isolated; page 7.26, first paragraph) with the added benefit that the RNA isolation column allows for the essential step of preparing mRNA for use in construction of cDNA libraries (page 7.26, first paragraph).

It would therefore have been obvious to modify the method of preparing an RNA sample as taught by Colpan et al with the precipitation and purification steps as taught by Sambrook et al as evidenced by Utermohlen and Stryer with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in rapid and quantitative concentration of the nucleic acid and would also have fulfilled the essential step of preparing mRNA for use in construction of cDNA libraries as explicitly taught by Sambrook et al (page E10, first paragraph and page 7.26, first paragraph).

While Colpan et al also teach DNA digestion (column 8, lines 61), neither Colpan et al not Sambrook et al teach digestion with DNAse after isolation of the precipitate.

However, Crossway et al teach a method of purification of nucleic acids (e.g., RNA; Abstract, lines 3-5) using digestion with DNAse with the added benefit of allowing differential detection of RNA only (column 5, lines 60-63).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the method of isolating a nucleic acid as taught by Colpan et al and Sambrook et al as evidenced by Utermohlen and Stryer with the DNAse treatment as taught by Crossway et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in allowing differential detection of RNA only as explicitly taught by Crossway et al (column 5, lines 60-63).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 1 and 3 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of copending Application No. 10/804,938 in view of Sambrook et al (*Molecular Cloning, A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15, pp. 7.26-7.29, and pp. E10-E.14 (1989)) as evidenced by Utermohlen (U.S. Patent No. 5,437,976, issued 1 August 1995) and Stryer (Biochemistry, 2nd ed, W.H.Freeman and Co., New York, page 376 (1981)).

Although the conflicting claims are not identical, both sets of claims are drawn to preparing an RNA sample, adding an organic solvent to the RNA sample, contacting said sample with an isolation column comprising a membrane, and eluting the RNA sample. The claims of the '938 application do not specify how the cRNA sample is prepared.

However, Sambrook et al also teach contacting an RNA isolation membrane column with said RNA-containing precipitate (e.g., performing oligo(dT) -cellulose type chromatography on the RNA; page 7.15, paragraph ii), wherein said column comprises a polymeric RNA isolation membrane (e.g.,

Amersham Hybond-mAP paper filters embedded with poly(U) residues [page 7.29, paragraph 2]; Utermohlen defines Hybond-mAP paper filters as comprising poly-U bound to arylamine substituted cellulose paper [column 3, lines 30-36],and Wade defines cellulose as a polymer [page 376, paragraph 5]; therefore, the Amersham Hybond-mAP paper filters are polymeric membranes) acting as a physical barrier to said RNA-containing precipitate and retaining the RNA-containing precipitate for purification (e.g., the membrane [i.e., the Amersham Hybond-mAP paper filter] is a physical barrier[i.e., a filter] that retains RNA; page 7.29, paragraph 20) with the added benefit that the RNA isolation column allows for the essential step of preparing mRNA for use in construction of cDNA libraries (page 7.26, first paragraph).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to modify the claims of the '938 application with the prefiltration procedure as taught by Sambrook et al as evidenced by Utermohlen and Stryer with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in rapid and quantitative concentration of the nucleic acid and would also have fulfilled the essential step of preparing mRNA for use in construction of cDNA libraries as explicitly taught by Sambrook et al (page E10, first paragraph and page 7.26, first paragraph).

This is a provisional obviousness-type double patenting rejection.

2. Claims 19-22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of copending Application No. 10/914,920 in view of Sambrook et al (*Molecular Cloning, A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15, pp. 7.26-7.29, and pp. E10-E.14 (1989)) as evidenced by Utermohlen (U.S. Patent No. 5,437,976, issued 1 August 1995) and Stryer (Biochemistry, 2nd ed, W.H.Freeman and Co., New York, page 376 (1981)).

Both sets of claims are drawn to methods form preparing an RNA sample comprising the steps of contacting a prefiltration column with a tissue lysate, wherein said prefiltration column has a fiber material comprising at least one layer of glass or borosilicate fiber, contacting the RNA sample with an RNA isolation column, and eluting said RNA from said column. The claims of the '920 Application are silent with respect to precipitation with an organic solvent and an RNA isolation membrane.

However, Sambrook et al also teach contacting an RNA isolation membrane column with said RNA-containing precipitate (e.g., performing oligo(dT) -cellulose type chromatography on the RNA; page 7.15, paragraph ii), wherein said column comprises a polymeric RNA isolation membrane (e.g., Amersham Hybond-mAP paper filters embedded with poly(U) residues [page 7.29, paragraph 2]; Utermohlen defines Hybond-mAP paper filters as comprising poly-U bound to arylamine substituted cellulose paper [column 3, lines 30-36],and Wade defines cellulose as a polymer [page 376, paragraph 5]; therefore, the Amersham Hybond-mAP paper filters are polymeric membranes) acting as a physical barrier to said RNA-containing precipitate and retaining the RNA-containing precipitate for purification (e.g., the membrane [i.e., the Amersham Hybond-mAP paper filter] is a physical barrier[i.e., a filter] that retains RNA; page 7.29, paragraph 20) with the added benefit that the RNA isolation column allows for the essential step of preparing mRNA for use in construction of cDNA libraries (page 7.26, first paragraph).

It would therefore have been obvious to modify the method of preparing an RNA sample as claimed in the '920 Application with the precipitation and purification steps as taught by Sambrook et al as evidenced by Utermohlen and Stryer with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in rapid and quantitative concentration of the nucleic acid and would also have fulfilled the essential step of preparing mRNA for use in construction of cDNA libraries as explicitly taught by Sambrook et al (page E10, first paragraph and page 7.26, first paragraph).

This is a provisional obviousness-type double patenting rejection.

Response to Arguments

Applicant's arguments filed 15 June 2006 have been fully considered but they are not persuasive for the reasons listed below.

1. Applicant argues on page 9 of the Remarks filed 15 June 2006 (i.e., "the Remarks") that the membrane of Sambrook et al is not the same as the instantly claimed membrane because the membrane of Sambrook et al is an affinity membranes, whereas the instantly claimed membrane acts as a physical barrier to said RNA-containing precipitate and plays a passive role in separating RNA.

However, independent claims 1 and 19 do not explicitly recite a passive role; rather the claims are drawn to "a polymeric membrane acting as a physical barrier to said RNA-containing precipitate and retaining the RNA-containing precipitate for purification." Applicant has cited page 18, third paragraph to page 19, first paragraph of the Specification for support of this limitation. Paragraph 1 of page 19 of the Specification specifically states:

> Although the membrane material plays a passive role, acting as a physical barrier to the precipitate, the nature of the polymeric material is important for efficient precipitate collection and to reduce absorptive losses. For example, comparison of various pore sizes of membranes results in changes in the mass recovery of RNA. Similarly, comparison of membranes prepared from different polymeric constituents also varies the mass recovery of RNA.

Therefore, as stated in the above paragraph, the only requirement necessary for the membrane to act in a passive role is to act as a physical barrier to the RNA-containing precipitate.

Sambrook et al teach a polymeric membrane acting as a physical barrier to said RNA-containing precipitate and retaining the RNA-containing precipitate for purification (e.g., the membrane [i.e., an Amersham Hybond-mAP paper filter] is a physical barrier [i.e., a filter] that retains RNA; page 7.29, paragraph 20). Thus, the claim has been given the broadest reasonable interpretation consistent with the Specification (*In re Hyatt*, 211 F.3d1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000) (see MPEP 2111 [R-1]). The additional teachings of the Specification regarding pore sizes and different polymeric constituents are clearly indicated as **examples,** but not as absolute structural requirements of the claimed

membranes. Because the membranes as taught by Sambrook et al meet the all of the limitations of the claimed membranes, the claimed membranes are anticipated by Sambrook et al.

2. Applicant also argues on page 10 of the Remarks that the polymeric membranes are not described able being specifically derivatized with nucleic acid moieties for increasing RNA-binding affinity. However, the additional structural elements of the membranes of Sambrook et al are encompassed by the open claim language "comprising" in the instant claims.

3. Applicant also argues on page 10 of the Remarks that the Specification teaches that the nature of the polymeric material is selected to reduce absorptive losses of RNA. However, independent claims 1 and 19 do not recite any limitations defining how the membrane reduces absorptive losses. In addition, Sambrook et al clearly teach that the membranes have minimal absorptive losses (e.g., the membranes are extremely useful when isolating small amounts or RNA; age 7.29, lines 7-11). Therefore, the membranes of Sambrook et al have minimal absorptive losses.

4. Applicant argues on page 11 of the Remarks that with neither Colpan et al nor Sambrook et al teaches an RNA isolation method wherein the mechanism of separation is precipitation.

However, independent claims 1 and 19 are merely require a polymeric membrane acting as a physical barrier to and retaining the RNA-containing precipitate. The precipitate of claims 1 and 19 is formed by the addition of an organic solvent to a sample preparation (claim 1) or filtrate (claim 19); hence the RNA-containing precipitate must be formed before contacting an RNA isolation membrane column as required by the claim.

The formation of an RNA-containing precipitate that is retained on a column is taught by Colpan et al (e.g., a column is washed with a buffer containing isopropanol [Example 1, column 8, lines 4-10] wherein nucleic acids are precipitated on the surface of the glass fibers [column 2, lines 12-17], and

collecting the effluent from said column, wherein said effluent is substantially free of said genomic DNA [i.e., RNA is purified]; column 6, lines 4-8).

Sambrook et al as evidenced by Utermohlen and Stryer also teach the formation of an RNA-containing precipitate wherein total cytoplasmic RNA is precipitated after removal of genomic DNA (e.g., gDNA is removed by precipitation [page 7.15, paragraph ii] prior to chromatography; page 7.26, paragraph 1) followed by contacting an RNA isolation membrane column with said RNA-containing precipitate (e.g., performing oligo(dT) -cellulose type chromatography on the RNA; page 7.15, paragraph ii), wherein said column comprises a polymeric RNA isolation membrane (e.g., Amersham Hybond-mAP paper filters embedded with poly(U) residues [page 7.29, paragraph 2]; Utermohlen defines Hybond-mAP paper filters as comprising poly-U bound to arylamine substituted cellulose paper [column 3, lines 30-36],and Wade defines cellulose as a polymer [page 376, paragraph 5]; therefore, the Amersham Hybond-mAP paper filters are polymeric membranes) acting as a physical barrier to said RNA-containing precipitate and retaining the RNA-containing precipitate for purification (e.g., the membrane [i.e., the Amersham Hybond-mAP paper filter] is a physical barrier[i.e., a filter] that retains RNA; page 7.29, paragraph 20).

Therefore, both Colpan et al and Sambrook et al teach the formation or RNA-containing precipitates by addition of organic solvents, followed by purification on a column. Sambrook et al provide motivation for modifying the method of Colpan et al with a second purification of the RNA-containing precipitate on a polymeric membrane (e.g., precipitation results rapid and quantitative concentration of the nucleic acid and the RNA-isolation membrane column provides the essential step of preparing mRNA for use in construction of cDNA libraries as explicitly taught by Sambrook et al (page E10, first paragraph and page 7.26, first paragraph), thereby meeting all of the limitations of the instant claims.

5. The remaining arguments of the Remarks regarding dependent claims 3-18 and 20-24 rely on arguments set forth to address the rejections of independent claims 1 and 19 under 35 USC 102(b) and 35 USC 103(a). Since these arguments were not persuasive, the rejections are maintained.

Conclusion

1. No claim is allowed

2. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

3. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571) 272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Robert T. Crow
Examiner
Art Unit 1634

JULIET C. SWITZER
PRIMARY EXAMINER